LOWER EXTREMITY PERIPHERAL ARTERY DISEASE AND QUALITY OF LIFE AMONG OLDER INDIVIDUALS IN THE COMMUNITY: THE ATHEROSCLEROSIS RISK IN COMMUNITIES (ARIC) STUDY

by Aozhou Wu

Department of Epidemiology

Johns Hopkins Bloomberg School of Public Health

A thesis submitted to Johns Hopkins University in conformity with the requirements for the degree of Master of Health Science

Baltimore, Maryland
April, 2015

ABSTRACT

Background: Lower extremity peripheral arterial disease (PAD), commonly identified by an ankle-brachial Index (ABI) <0.9, increases mortality risk and may impair quality of life (QOL). However, most studies assessing reduced QOL in the relation to PAD rely on small clinical studies, leaving uncertainty about the impact of PAD on QOL in the community.

Methods: Using data of 5,115 ARIC visit 5 (2011-2013) participants aged 66-90 years, we assessed the associations of ABI with several QOL parameters, including physical and mental components in SF-12 as well as some other QOL parameters (leisure time exercise/activity/walking, depression, and hopeless feeling. We used linear/logistic regression models to adjust for demographic characteristics, cardiovascular disease (CVD) risk factors, history of CVD, and other comorbidities including lung disease and reduced kidney function.

Results: There were 402 participants with low ABI < 0.90 and 426 participants with borderline low ABI (0.90-0.99). Overall, there were dose-response relationships between lower ABI and poor status of QOL parameters. With ABI 1.10-1.19 as a reference (n=1900), the associations of low ABI (< 0.90) and impaired QOL were much more evident in physical components (Physical Component Summary: -3.27 [95%CI: -5.60 to -0.93]), compared to mental components (Mental Component Summary: -0.07 [95%CI:

-2.21 to 2.06]). Regarding each of eight domains in SF-12, low ABI was significantly associated with all four domains for physical components (Physical Functioning, Role Physical, Bodily Pain, and General Health) but only with one of four domains for mental components (vitality). Similarly low ABI was more consistently associated with the other physical QOL parameters than the other mental parameters. Interestingly, a poor status of several QOL parameters was also observed in borderline low ABI. Similar results for lower ABI and physical QOL parameters were observed in subgroups according to sex, race as well as history of CVD, diabetes, and reduced kidney function.

Conclusions: Lower ABI was independently associated with poor status of QOL, especially on physical, with potential important implications on quality-maintained life in older individuals. Further studies are warranted to assess if the PAD-specific management can improve QOL among individuals with lower ABI.

Advisor: Josef Coresh, MD

Thesis reader: Kunihiro Matsushita, MD

PREFACE

Peripheral artery disease (PAD) has high prevalence in older population. Usually combined with other cardiovascular comorbidities, PAD patients' prognoses are not optimistic. On the other hand, PAD itself could affect patients' moving ability and may reduce their quality of life (QOL). This study focused on the impact of PAD on quality of life in general older populations. Using ankle-brachial index (ABI) as an indicator, we explored the potential quantitative association between ABI and multiple health-related QOL elements and wished to provide some advices on QOL management in PAD patients and also help generate further hypothesis on PAD-QOL association in the future study.

Acknowledgement

We thank the patients, staff, researchers, and laboratory for their participation in the ARIC Study. National Heart, Lung, and Blood Institute (NHLBI) funds the study by contracts: N01-HC-55015, N01-HC-55016, N01-HC-55018, N01-HC-55019, N01-HC-55020, N01-HC-55021, and N01-HC-5502. The neurocognitive data is supported by U01 HL096812, HL096814, HL096899, HL096902, and HL096917.

CONTENTS

LIST OF TABLES

Main Tables

Supplementary Tables

LIST OF FIGURE

INTRODUCTION

Peripheral arterial disease (PAD), commonly identified by an ankle brachial index (ABI) less than 0.9, is increasingly important,[1] especially in older adults. In the US, PAD affects over 8 millions individuals,[2] including about 20% of people aged over 70 years.[3, 4] Persons with PAD have 3 to 5 fold higher mortality risk compared with those without PAD, which is mainly due to higher risk of cardiovascular diseases (CVD),[5-7] reflecting the property of PAD as a manifestation of systemic atherosclerosis.[8]

PAD also has impact on quality of life (QOL). As the disease progresses, patients with PAD may develop intermittent claudication and critical limb ischemia (a condition including ischemic rest pain, ulcers, or gangrene, with up to 25% of amputation risk within one year after diagnosis),[9] leading to reduction of health-related QOL. Indeed, several studies confirm this aspect of PAD,[10-15] but these results came from small studies or predominantly investigated clinical population mainly with symptomatic PAD, leaving uncertainty about the impact of PAD on QOL in the community.

Therefore, the aim of this study is to comprehensively investigate the full spectrum of ABI and its association with health-related QOL among older adults in the community using data from the Atherosclerosis Risk in Communities Study (ARIC) Study. Since the relative importance of QOL over prognosis becomes larger as one ages[16] and PAD-specific management (e.g., supervised exercise) has been shown to improve QOL,

our findings would have clinical and public health implications.

METHODS

Study Population

The ARIC Study is an ongoing prospective cohort to investigate the natural history of atherosclerosis and related cardiovascular event and consists of 15,792 participants aged 45–64 at baseline visit in 1987–1989 from four U.S. communities, Forsyth County, North Carolina, Jackson, Mississippi, suburbs of Minneapolis, Minnesota, and Washington County, Maryland. The ARIC Study conducted fifth examination between June 1st, 2011 and August 30th, 2013, at which 6,538 participants aged 66-90 years attended. Of these visit attendees, we excluded 18 non-Caucasian/non-African American participants, and additional 868 participants without ABI measurement. In addition, 537 participants with missing information for covariates and QOL data were further excluded, leaving the final population of 5,115 participants for this study.

ABI Measurement

Ankle-brachial index was defined as the ratio of systolic blood pressure in the ankle divided by the systolic pressure in the arm. Using an oscillometric device, OMRON VP-1000 plus (Kyoto, Japan), blood pressure was automatically and simultaneously measured in both ankles and arms by trained and certified technicians.[17] Using higher value of right and left arm blood pressure as denominator, ABI was calculated for right and left legs. The measurement was repeated after five minutes, and the mean ABI was

recorded for right and left legs. The lower value of right and left ABI was used for this analysis in general. One exception was when both ABIs are greater than 1.0 and at least one ABI was higher than 1.3. In this scenario, to capture pathophysiological information of high ABI (indicating arterial stiffness and calcification),[2, 18-20] we used higher ABI value for our analysis.

Health-related quality of life (QOL)

Our primary measure of health-related QOL relied on 12-item Short-Form Health Survey (SF-12), which captures both physical and mental elements of health-related QOL. To assess the robustness of our findings, we also evaluated physical activity and hopeless feeling based on self-report and depression based on the Epidemiologic Studies Depression Scale (CES-D) Short Form.

12-item Short-Form Health Survey (SF-12)

SF-12 questionnaire is designed for health-related QOL assessment that has been validated across populations,[21, 22] and is comparable to the original full form of SF-36.[21, 23] It reports two summary measurements for physical and mental health-related QOL, i.e., Physical Component Summary and Mental Component Summary. Each summary component was based on four domains: Physical Component Summary - physical functioning (the ability to do moderate activities / climb stairs), role-physical (impaired working ability / daily activities due to physical issue), bodily pain (extend to which pain

interfere daily work), and general health (self-grading health status); Mental Component Summary - mental health (whether feel peaceful or depressed), role-emotional (impaired working ability / daily activities due to emotional issue), social functioning (frequency of social activities interfered by physical/emotional issues), and vitality (whether feel energetic). Although detailed calculation for QOL score can be found elsewhere,[24] briefly, QOL score between 0 and 100 for each domain was given to each participant according to one or several questions with 3 or 5 points scale and high score indicates high QOL. The QOL score is standardized to general U.S. population with a mean of 50 and a standard deviation of 10.

Other health-related QOL variables

Leisure time exercise frequency, activity level comparing to peers, and walking frequency were collected with questionnaire during interview. We defined participants who reported "never" or "seldom" for leisure time exercise as "low" leisure time exercise (n=2,483) and defined those reported "much less" or "less" for leisure time activity level comparing to peers as "low" leisure time activity (n=900). We also defined participants who reported "never" or "seldom" for leisure time walking frequency as "low" leisure time walk (n=1,507).

The CES-D Short Form is a depression related symptom measurement instrument, with 11 items selected from the full CES-D Form with 20 items and demonstrates good

validity[25] and high correlation with the full CES-D Form (Pearson r = 0.95).[26] With a scale between 0 and 2 (0 = hardly ever or never; 1 = some of the time; 2 = much or most of the time) for each item, the total CES-D score can be between 0 and 22. The score was treated as missing if more than 1 item were missing. Depression was defined as CES-D score ≥9 (n=310).[17] Information about the frequency of feeling hopeless in the past week (<1 day, 1-2 days, 3-7 days) was gathered via a simple question asking during the interview. Hopeless feeling was defined by having hopeless feeling at least 1 day in the previous week (n=520).

Covariates

Age, sex, ethnicity, were self-reported. Information of education level (high school or lower vs. college or above) was collected during ARIC visit 1 interview. Self-indicated economic status was based on self-estimated rank of family financial situation comparing to the whole US population, with 10 categories. Lower self-indicated economic status was defined as having a score < 6 (median score in the study participants). Body mass Index was calculated as weight (kg) divided by the square of height (m). Total cholesterol was assessed via enzymatic methods.[27] Glucose level was measured by hexokinase/glucose-6-phosphate dehydrogenase methods.[28] Diabetes was defined as fasting glucose level ≥126 mg/dL (or 7 mmol/L), non-fasting glucose level ≥200 mg/dL (or 11.1 mmol/L), medication use for diabetes, or self-reported physician diagnosis.

Hypertension was defined as systolic blood pressure (mean of the 2nd and 3rd measurements in sitting position) ≥140 mmHg or diastolic blood pressure ≥90 mmHg or use of anti-hypertensive medication. History of coronary heart disease and stroke was identified by the clinical history acquired at visit 1 and CHD and stroke events between visits 1 and visit 5, respectively. History of heart failure (HF) was defined as definite, probable, or chronic stable HF by an ARIC physician adjudication panel or hospitalization with ICD code 428.x prior to Visit 5, HF diagnosis confirmed with participants' physicians. Lung disease was based on the self-reported physician diagnosis of emphysema/chronic obstructive pulmonary disease, chronic bronchitis or asthma. Estimated glomerular filtration rate (eGFR) was derived using the CKD-EPI equation incorporating serum creatinine level, sex, race, and age.[29] Reduced kidney function was defined as eGFR <60 mL/min/1.73m^2.[29]

Statistical Analysis

According to clinical guidelines and previous literature,[20, 30, 31] ABI value was categorized into six groups: <0.90, 0.90-0.99, 1.00-1.09, 1.10-1.19, 1.20-1.29, ≥1.30. The category of 1.10-1.19 was used as reference since it was the most prevalent category in our study and was used as a reference in a previous meta-analysis.[32] Participants' baseline characteristics were compared across these six ABI groups based on chi-square tests and ANOVA tests, as appropriate. We ran linear regression models for continuous QOL

parameters from SF-12 (two summary components and eight health-related domains) and logistic regression models for the other QOL variables related to leisure time physical activity and mental status ("low" leisure time exercise/activity/walking, depression and hopeless feeling). To evaluate the influence of potential confounders, three models were constructed. Model 1 adjusted for demographic variables, age, sex, ethnicity, education level, and self-indicated economics status. Model 2 further adjusted for CVD risk factors (current smoking/drinking status, body mass index, total cholesterol level, diabetes, hypertension) and history of CVD (history of CHD, heart failure and stroke). Model 3 additionally included the presence of lung disease and reduced kidney function. Since we are particularly interested in the independent association of ABI with health-related QOL, we primarily demonstrate results based on Model 3. We repeated the analysis in subgroups according to sex, race, and the status of CVD history, diabetes, and reduced kidney function. In this subgroups analysis, we kept six ABI categories for continuous QOL parameters but, to obtain reliable estimates, analyzed dichotomous ABI (<1.00 and ≥1.00 as reference) for dichotomous QOL parameters. $P < 0.05$ was considered statistically significant.

RESULTS

Participants' characteristics

The mean age of 5,115 participants was 75.4 (SD 5.0) years, and 21.8% (n=1,113) were African American. There were 402 participants (7.9%) with low ABI <0.90, a category considered as PAD, and 426 (8.3%) with borderline low ABI of 0.90-0.99. As compared to participants with ABI 1.10-1.19, those with lower ABI tended to have worse cardiovascular risk factor profile, namely older age, lower socioeconomic status, higher prevalence of current smokers, diabetes, hypertension, history of cardiovascular, lung disease and reduced kidney function (Table 1). Those with high ABI (≥1.30) also demonstrated worse profile for some risk factors and clinical conditions such as older age, higher adiposity, and higher prevalence of diabetes, and prior history of cardiovascular disease compared to those with ABI 1.10-1.19.

12-item Short-Form Health Survey (SF-12)

In the overall study population, the mean score for Physical/Mental Component Summary was 46.8 (SD 9.9) and 55.5 (SD 7.5), respectively (Supplementary Table 1.). With the reference of ABI 1.10-1.19, ABI categories <1.00 demonstrated significantly lower score for Physical Component Summary (-3.26 [95%CI: -5.60 to -0.92] for ABI <0.90 and -2.23 [95%CI: -4.07 to -0.39] for ABI 0.90-0.99). On the other hand, the difference was not evident for Mental Component Summary. (Figure 1) When we looked at each domain

separately, ABI <0.90 was significantly associated with lower score in all domains of physical components, compared to the reference, with most evident difference in physical functioning (-3.42 [95%CI: -5.50 to -1.35]) followed by role physical, general health and bodily pain (Table 2). ABI 0.90-0.99 showed lower score in all physical domains compared to the reference as well, but the difference reached significance only for “role physical” domain (-1.87 [95%CI: -3.58 to -0.16]) and bodily pain domain (-1.59 [95%CI: -3.13 to -0.05]). As anticipated, more evident dose-response association between lower ABI and reduced physical QOL domains were observed for Models 1 and 2 (Supplementary Table 2 and 3).

For mental components, the association was overall weaker than physical components but ABI categories <1.00 had significantly lower vitality score compared to the reference group (ABI 1.10-1.19) (-1.54 [95%CI: -2.25 to -0.83] for ABI <0.9 and -1.38 [95%CI -1.98 to -0.78] for ABI 0.90-0.99). Similar results were observed in Model 1 and 2 except for the presence of significant association between low ABI and role emotional domain as well as more evident ABI-vitality association. High ABI did not demonstrate significantly lower score in any of physical and mental domains.

The Other QOL parameters

We observed dose-response relationships between ABI and the other physical QOL parameters (Table 3). Consistent with the results for physical components in SF-12, low

ABI (<0.90) was significantly associated with all three physical activity parameters (OR: 1.34 [95%CI: 1.09 to 1.64] for “low” leisure time exercise, 1.35 [95%CI: 1.21 to 1.50] for “low” leisure time activity and 1.43 [95%CI: 1.25 to 1.63] for “low” leisure time walk) compared to the reference ABI. The significant impairments on leisure time activity level and walking frequency were also observed in borderline low ABI 0.90-0.99. Of note, low normal ABI 1.00-1.09 was also significantly associated with the three physical activity parameters (OR: 1.21 [95%CI: 1.09 to 1.35] for “low” leisure time exercise, 1.15 [95%CI: 1.04 to 1.26] for “low” leisure time activity and 1.24 [95%CI: 1.11 to 1.39] for “low” leisure time walk). More evident associations were observed in Models 1 and 2. (Supplementary Table 4 and 5)

The other mental parameters demonstrate weaker associations with lower ABI compared to the other physical parameters (Table 3). Although a general dose-response relationship was observed for depression, none of the odds ratios were significant for low ABI categories. The odds of hopeless feeling were only significantly higher in borderline low ABI 0.90-0.99 compared to the reference ABI.

Subgroup analysis

Overall, dose-response associations with lower ABI (<1.00) were observed for poor physical QOL components based on SF-12 in most subgroups tested (Supplementary Table 6), but not for mental QOL components (Supplementary Table 7). Notably, for the

other physical QOL parameters, the association between lower ABI and lower leisure time exercise, activity, and walking was consistently more evident in participants without history of CVD than in those with history of CVD with significant interaction for “low” leisure time activity (p for interaction = 0.007) and “low” leisure time walk (p for interaction < 0.001) (Supplementary Table 8). Similar pattern was observed for reduced kidney function status. In addition relatively stronger association between lower ABI and impaired physical actives parameters was found in Caucasian compared to African American, but the effect modification was not significant.

For mental components, reflecting overall weak association with ABI, the association was not evident in any subgroups except within some racial groups for depression and hopeless feeling. Specifically, lower ABI (<1.00) was associated with higher odds of depression and hopeless feeling compared to ABI ≥1.00 in Caucasian, whereas lower ABI was related to lower odds of those mental conditions in African American. (Supplementary Table 9)

DISCUSSION

This study quantified the association between ABI values and several domains of QOL among community-dwelling older adults in the US. With ABI 1.10-1.19 as reference group, low ABI <0.90 and borderline low ABI (0.90-0.99) were associated with poorer status of QOL parameters, with general dose-response relationship. The contribution of lower ABI was more evident for physical components of QOL than for mental components in SF-12. The association of ABI with physical QOL was confirmed in other parameters such as leisure time exercise, activity, and walking as well. Of note, lower ABI was significantly associated with a mental domain, vitality. Notably, poor QOL status for physical components was observed even among those without other CVD (i.e., coronary disease, stroke, and heart failure) or clinical conditions tightly related to PAD (e.g., diabetes and reduced kidney function).

The more evident association of low ABI with physical components of QOL status than mental components is consistent with previous studies investigating clinical populations.[33-35] Of note, our study is first to confirm this aspect in community-dwelling older adults not selected for clinical conditions and hence not susceptible to spectrum bias. There are several potential mechanisms linking PAD to the impairments for physical components of QOL. Individuals with low ABI often have other CVDs and comorbidities, which may reduce QOL. However, the association of ABI with physical domains of QOL

was independent of those comorbidities. In terms of PAD-specific potential mechanisms, decreased blood flow to leg can induce skeletal muscle atrophy and denervation through repeated ischemia.[36] Leg pain or discomfort can additionally contribute to limited physical ability. In addition, fear of falling was reported among those with intermittent claudication[37] and could further impact physical activity.

Although weaker than physical domains, low ABI was significantly associated with a mental element of QOL, i.e., vitality, in our study, which is in line with previous studies showing stronger association of low ABI with vitality than other mental domains. We observed a higher odds of hopeless feeling in ABI 0.90-0.99 compared to ABI 1.10-1.19, but we should interpret this result with caution since we did not necessarily observe higher odds in ABI <0.9. Although the exact mechanisms for PAD to impact vitality are not clear, limited physical activity as well as working ability due to PAD may play a role. Also, aforementioned leg pain or fear of falling due to PAD may contribute to reduced mental elements of QOL.

Although a weaker association was seen among individuals with history of CVD than those without, the contribution of low ABI to physical QOL parameters was qualitatively consistent across all subgroups tested in our study. The weaker association among those with history of CVD may be due to the fact that many participants with prior CVD had reduced QOL and ABI may not considerably contribute to further discrimination beyond other CVDs. Similar Effect modification was observed for reduced kidney function

status. On the other hand, we observed a significant qualitative racial interaction for low ABI and depression/hopeless feeling, with positive associations in Caucasian but negative relations in African American. The potential background for this significant interaction was not clear, but we should keep in mind that we tested five subgroups without a priori hypothesis for the direction of interaction and there were relatively small number of African American in our study. Thus, our results should be considered hypothesis generating and confirmation in other settings is needed.

Our findings of the association of low ABI and impaired QOL among community-dwelling older adults may have some clinical and public health implications. Maintaining physical activity is an important element for older adults' ability to sustain independent living. Since several lifestyle (e.g., smoking cessation or supervised-exercise) or medical (e.g., Cilostazol or revascularization) interventions have demonstrated to improve physical function in PAD patients, it seems important to identify the contribution of PAD, if any, to the reduction of physical-related QOL in older adults. It is important to keep in mind that reduced QOL was also observed in those with borderline low ABI in our study. Further studies would be needed to assess whether the aforementioned PAD-specific interventions would comprehensively improve physical-related QOL as well as vitality in those with low ABI.

There are several limitations in our study. First, given a cross-sectional analysis, we cannot infer temporality for low ABI and poor QOL status. Second, it is possible that

those with very low ABI and/or severely reduced QOL could not attend ARIC visit 5, raising possibility that our results may underestimate the ABI-QOL relationship. Third, the ARIC Study did not collect information on leg pain at visit 5. Fourth, generalization of our findings to racial/ethnic groups other than Caucasian and African American needs to be done carefully. Finally, as true in any observational studies, we cannot deny the possibility of residual confounding.

In conclusion, among older adults in the community, low ABI and borderline low ABI were associated with poor QOL status. The association was particularly evident for physical components of QOL, but a mental domain, vitality, was associated with low ABI as well. Further studies are warranted to evaluate the causality of ABI in the reduction of QOL and, if so, to explore whether the management of PAD improves QOL among individuals with low ABI.

APPENDICES

Main Tables

Table 1. Participant's characteristics description across ABI categories

Characteristics	ABI categories† (n)							
	All (5,115)	<0.9 (402)	0.90-0.99 (426)	1.00-1.09 (1,234)	1.10-1.19 (1,900)	1.20-1.29 (694)	≥1.3 (459)	P-value
Age, mean (SD)	75.4 (5.0)	77.3 (5.5)	76.0 (5.6)	75.3 (5.1)	75.0 (4.8)	74.8 (4.9)	75.5 (4.8)	<0.001
Sex (Females)	2948 (57.6%)	214 (53.2%)	298 (70.0%)	878 (71.2%)	1138 (59.9%)	289 (41.6%)	131 (28.5%)	<0.001
Ethnicity (African American)	1113 (21.8%)	164 (40.8%)	133 (31.2%)	352 (28.5%)	352 (18.5%)	66 (9.5%)	46 (10.0%)	<0.001
Lower Education Level	2819 (55.1%)	258 (64.2%)	264 (62.0%)	732 (59.3%)	1029 (54.2%)	339 (48.8%)	197 (42.9%)	<0.001
Lower self-indicated economic status	2367 (46.3%)	232 (57.7%)	229 (53.8%)	642 (52.0%)	828 (43.6%)	267 (38.5%)	169 (36.8%)	<0.001
Current Smoker	2805 (58.0%)	274 (73.7%)	249 (62.4%)	662 (56.8%)	1003 (55.8%)	352 (53.3%)	265 (60.0%)	<0.001
Current Drinker	4059 (79.4%)	314 (78.1%)	328 (77.0%)	933 (75.6%)	1537 (80.9%)	571 (82.3%)	376 (81.9%)	<0.001
Body Mass Index, mean (SD)	28.6 (5.5)	28.9 (5.9)	29.5 (6.6)	29.0 (5.7)	28.2 (5.1)	28.0 (4.7)	29.1 (5.6)	<0.001
Total Cholesterol, mean (SD)	4.7 (1.1)	4.6 (1.1)	4.8 (1.1)	4.8 (1.1)	4.7 (1.1)	4.6 (1.0)	4.4 (1.0)	<0.001
Diabetes	1606 (31.4%)	173 (43.0%)	142 (33.3%)	388 (31.4%)	546 (28.7%)	205 (29.5%)	152 (33.1%)	<0.001
Hypertension	3774 (73.8%)	347 (86.3%)	338 (79.3%)	953 (77.2%)	1343 (70.7%)	481 (69.3%)	312 (68.0%)	<0.001
CHD History	734 (14.3%)	115 (28.6%)	72 (16.9%)	153 (12.4%)	229 (12.1%)	88 (12.7%)	77 (16.8%)	<0.001
Heart Failure History	239 (4.7%)	58 (14.4%)	28 (6.6%)	56 (4.5%)	59 (3.1%)	16 (2.3%)	22 (4.8%)	<0.001
Stroke History	174 (3.4%)	29 (7.2%)	26 (6.1%)	36 (2.9%)	50 (2.6%)	18 (2.6%)	15 (3.3%)	<0.001
Lung Disease	566 (11.1%)	72 (17.9%)	64 (15.0%)	155 (12.6%)	185 (9.7%)	54 (7.8%)	36 (7.8%)	<0.001
Reduced Kidney Function	1424 (27.8%)	176 (43.8%)	160 (37.6%)	351 (28.4%)	463 (24.4%)	156 (22.5%)	118 (25.7%)	<0.001

Table 2. The difference in QOL scores across ABI categories.

QOL Domains	ABI categories† (n)					
	<0.90 (402)	0.90-0.99 (426)	1.00-1.09 (1,234)	1.10-1.19 (1,900)	1.20-1.29 (694)	≥1.30 (459)
	Coefficient$^{\Delta}$ (95% CI)	Coefficient (95% CI)	Coefficient (95% CI)	Ref	Coefficient (95% CI)	Coefficient (95% CI)
Physical Components	**-3.26 (-5.60 to -0.92)**	**-2.23 (-4.07 to -0.39)**	-0.62 (-1.42 to 0.19)	0	-0.56 (-1.71 to 0.59)	-0.13 (-1.09 to 0.82)
Physical Functioning	**-3.42 (-5.50 to -1.35)**	-1.71 (-3.94 to 0.52)	-0.68 (-1.58 to 0.22)	0	-0.21 (-1.61 to 1.18)	-0.43 (-1.58 to 0.71)
Role Physical	**-2.76 (-4.98 to -0.55)**	**-1.87 (-3.58 to -0.16)**	-0.90 (-2.25 to 0.45)	0	-0.45 (-1.48 to 0.58)	-0.01 (-1.64 to 1.62)
Bodily Pain	**-1.99 (-3.77 to -0.22)**	**-1.59 (-3.13 to -0.05)**	-0.15 (-0.81 to 0.52)	0	-1.01 (-2.48 to 0.45)	-0.03 (-1.42 to 1.35)
General Health	**-2.31 (-3.52 to -1.09)**	-1.55 (-3.30 to 0.20)	-0.16 (-1.36 to 1.04)	0	0.00 (-1.16 to 1.16)	0.50 (-0.63 to 1.63)
Mental Components	-0.07 (-2.21 to 2.06)	0.15 (-0.96 to 1.26)	0.06 (-0.54 to 0.66)	0	0.09 (-0.62 to 0.79)	0.37 (-0.44 to 1.19)
Mental Health	-0.62 (-2.47 to 1.23)	0.01 (-0.51 to 0.53)	0.29 (-0.59 to 1.17)	0	0.04 (-1.15 to 1.23)	0.47 (-0.64 to 1.57)
Role Emotional	-1.41 (-2.98 to 0.16)	-0.42 (-1.49 to 0.64)	-0.74 (-1.49 to 0.00)	0	-0.13 (-0.91 to 0.65)	-0.17 (-0.97 to 0.64)
Social Functioning	-0.58 (-2.07 to 0.92)	-0.54 (-1.99 to 0.92)	0.02 (-0.42 to 0.46)	0	-0.02 (-1.23 to 1.19)	0.09 (-1.27 to 1.45)
Vitality	**-1.54 (-2.25 to -0.83)**	**-1.38 (-1.98 to -0.78)**	-0.18 (-0.49 to 0.13)	0	-0.31 (-0.88 to 0.26)	0.42 (-0.03 to 0.88)

Δ Linear regression coefficient: It represents the difference in QOL score between a given ABI category to the reference category (1.10-1.19), adjusted for all covariates. Negative coefficient means lower QOL score in the given category comparing to the reference group. Red & bold indicates statistically significant results.

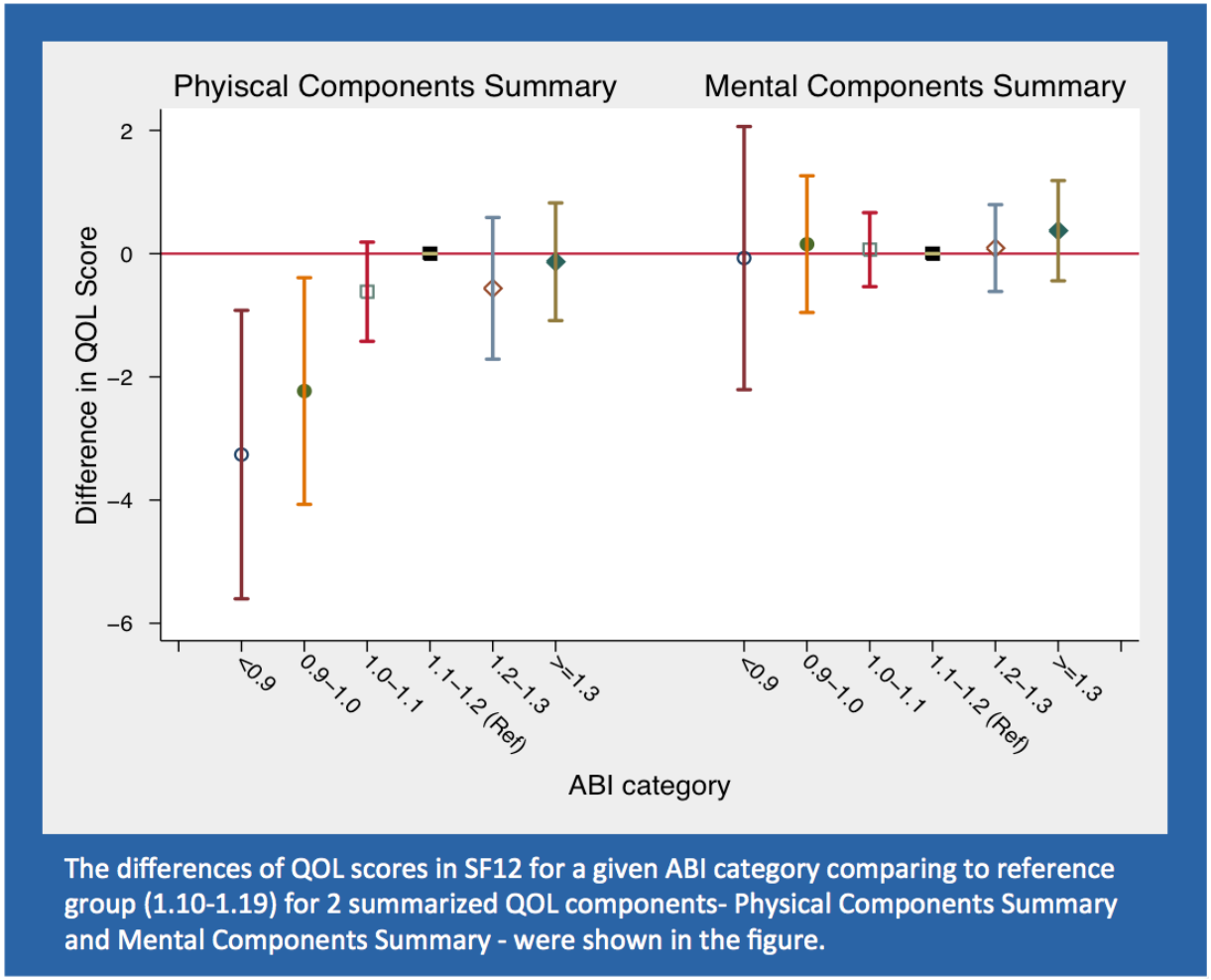
Table 3. Odds-ratio of other QOL parameters across ABI categories.

Other QOL Parameters	ABI categories† (n)					
	<0.90	0.90-0.99 (426)	1.00-1.09 (1,234)	1.10-1.19 (1,900)	1.20-1.29 (694)	≥1.30 (459)
	# low QOL/total OR$^{\Delta}$ (95% CI)	# low QOL/total OR (95% CI)	# low QOL/total OR (95% CI)	Ref	# low QOL/total OR (95% CI)	# low QOL/total OR (95% CI)
Physical Activity						
"Low" leisure time exercise	230/402 **1.34 (1.09 to 1.64)**	248/426 1.38 (0.98 to 1.93)	656/1,234 **1.21 (1.09 to 1.35)**	859/1,900 1	299/694 1.01 (0.79 to 1.30)	191/459 0.95 (0.68 to 1.32)
"Low" leisure time activity	101/402 **1.35 (1.21 to 1.50)**	103/426 **1.26 (1.13 to 1.40)**	253/1,234 **1.15 (1.04 to 1.26)**	304/1,900 1	80/694 **0.74 (0.62 to 0.88)**	59/459 **0.76 (0.60 to 0.98)**
"Low" leisure time walk	158/402 **1.43 (1.25 to 1.63)**	162/426 **1.38 (1.08 to 1.76)**	413/1,234 **1.24 (1.11 to 1.39)**	501/1,900 1	163/694 0.94 (0.77 to 1.14)	110/459 0.93 (0.80 to 1.08)
Mental Health						
Depression	46/402 1.51 (0.87 to 2.62)	35/426 1.19 (0.79 to 1.81)	91/1,234 1.22 (0.98 to 1.52)	95/1,900 1	24/694 0.79 (0.46 to 1.34)	19/459 0.91 (0.62 to 1.32)
Hopeless Feeling	55/402 1.13 (0.97 to 1.31)	56/426 **1.20 (1.07 to 1.33)**	159/1,234 1.32 (0.96 to 1.80)	165/1,900 1	50/694 0.91 (0.63 to 1.32)	35/459 0.94 (0.53 to 1.66)

Δ Logistic regressions were applied to assess the 5 binary other QOL parameters, adjusted for all covariates. Red & bold indicates statistically significant results.

Figure

Figure 1. The difference in QOL scores across ABI categories (Physical / Mental Component Summary from SF12).



The differences of QOL scores in SF12 for a given ABI category comparing to reference group (1.10-1.19) for 2 summarized QOL components- Physical Components Summary and Mental Components Summary - were shown in the figure.

Supplement Tables

Supplementary Table 1. Description of participant's SF-12 QOL parameters across ABI categories.

Characteristics	ABI categories† (n)							
	All (5,115)	<0.90 (402)	0.90-0.99 (426)	1.00-1.09 (1,234)	1.10-1.19 (1,900)	1.20-1.29 (694)	≥1.30 (459)	P-value
Physical Component†	46.8 (9.9)	41.9 (10.5)	43.6 (10.8)	46.3 (10.0)	48.1 (9.2)	48.2 (9.5)	48.1 (9.0)	<0.001
Physical Functioning†	47.9 (10.4)	43.0 (11.5)	45.1 (11.6)	47.2 (10.6)	49.0 (9.7)	49.7 (9.7)	49.0 (9.5)	<0.001
Role Physical†	48.5 (9.1)	44.5 (9.7)	46.1 (9.6)	47.9 (9.3)	49.6 (8.8)	49.6 (8.5)	49.5 (8.5)	<0.001
Bodily Pain†	48.7 (10.1)	46.1 (10.9)	46.5 (11.6)	48.5 (10.1)	49.5 (9.7)	49.0 (9.7)	49.8 (9.3)	<0.001
General Health†	50.1 (9.7)	44.8 (10.8)	47.1 (10.2)	49.5 (9.4)	51.2 (9.3)	52.1 (8.9)	52.2 (8.8)	<0.001
Mental Component †	55.5 (7.5)	54.6 (9.0)	55.1 (8.4)	55.2 (7.9)	55.5 (7.0)	56.0 (6.8)	56.4 (6.4)	0.002
Mental Health†	54.9 (7.9)	53.3 (9.1)	54.0 (8.8)	54.7 (8.0)	55.1 (7.6)	55.7 (7.1)	56.2 (7.0)	<0.001
Role Emotional†	51.9 (7.5)	49.7 (9.4)	51.1 (7.9)	51.1 (8.2)	52.5 (6.9)	52.7 (6.4)	52.6 (6.8)	<0.001
Social Functioning†	52.7 (7.9)	51.0 (9.5)	51.6 (8.7)	52.5 (8.0)	53.1 (7.8)	53.4 (7.0)	53.4 (6.9)	<0.001
Vitality†	53.1 (9.1)	50.4 (9.6)	50.9 (9.3)	52.8 (9.1)	53.8 (8.9)	53.9 (8.7)	54.3 (8.6)	<0.001

†: mean (SD) was reported.

Supplementary Table 2. The difference in QOL scores across ABI categories using Model 1†.

QOL Domains	ABI categories† (n)					
	<0.90 (402)	0.90-0.99 (426)	1.00-1.09 (1,234)	1.10-1.19 (1,900)	1.20-1.29 (694)	≥1.30 (459)
	Coefficient$^{\Delta}$ (95% CI)	Coefficient (95% CI)	Coefficient (95% CI)	Ref	Coefficient (95% CI)	Coefficient (95% CI)
Physical Components	**-5.28 (-8.32 to -2.24)**	**-3.72 (-5.03 to -2.41)**	**-1.29 (-1.82 to -0.75)**	0	-0.39 (-1.98 to 1.20)	-0.72 (-1.90 to 0.47)
Physical Functioning	**-5.41 (-8.11 to -2.71)**	**-3.17 (-5.02 to -1.33)**	**-1.33 (-2.12 to -0.55)**	0	-0.03 (-2.05 to 2.00)	-1.01 (-2.78 to 0.76)
Role Physical	**-4.33 (-7.14 to -1.52)**	**-3.03 (-4.01 to -2.04)**	**-1.41 (-2.34 to -0.48)**	0	-0.32 (-1.21 to 0.58)	-0.44 (-2.02 to 1.14)
Bodily Pain	**-3.21 (-5.24 to -1.19)**	**-2.60 (-4.34 to -0.85)**	**-0.61 (-0.94 to -0.29)**	0	-0.91 (-2.59 to 0.77)	-0.47 (-2.29 to 1.34)
General Health	**-4.12 (-5.97 to -2.26)**	**-2.71 (-4.26 to -1.17)**	-0.69 (-2.05 to 0.68)	0	0.14 (-1.26 to 1.54)	0.16 (-0.35 to 0.68)
Mental Components	-0.34 (-2.25 to 1.57)	-0.01 (-1.04 to 1.03)	0.00 (-0.60 to 0.61)	0	0.11 (-0.54 to 0.76)	0.37 (-0.51 to 1.26)
Mental Health	-1.24 (-2.84 to 0.36)	**-0.42 (-0.77 to -0.06)**	0.11 (-0.73 to 0.96)	0	0.11 (-1.00 to 1.21)	0.39 (-0.82 to 1.60)
Role Emotional	**-2.00 (-3.60 to -0.39)**	-0.83 (-2.10 to 0.43)	**-0.93 (-1.70 to -0.16)**	0	-0.09 (-0.93 to 0.75)	-0.32 (-1.44 to 0.79)
Social Functioning	-1.28 (-2.88 to 0.32)	-1.01 (-2.61 to 0.59)	-0.19 (-0.51 to 0.13)	0	0.05 (-1.23 to 1.34)	-0.07 (-1.52 to 1.39)
Vitality	**-2.89 (-4.54 to -1.25)**	**-2.41 (-3.11 to -1.71)**	-0.62 (-1.25 to 0.02)	0	-0.20 (-0.90 to 0.50)	0.05 (-0.83 to 0.94)

Δ Linear regression coefficient: It represents the difference in QOL score between a given ABI category to the reference category (1.10-1.19). Negative coefficient means lower QOL score in the given category comparing to the reference group. Red & bold indicates statistically significant results.

† Model 1 covariates: age, sex, ethnicity, education level, self-indicated economics status.

Supplementary Table 3. The difference in QOL scores across ABI categories using Model 2†.

QOL Domains	ABI categories† (n)					
	<0.90 (402)	0.90-0.99 (426)	1.00-1.09 (1,234)	1.10-1.19 (1,900)	1.20-1.29 (694)	≥1.30 (459)
	Coefficient$^{\Delta}$ (95% CI)	Coefficient (95% CI)	Coefficient (95% CI)	Ref	Coefficient (95% CI)	Coefficient (95% CI)
Physical Components	**-4.40 (-6.88 to -1.92)**	**-2.82 (-4.28 to -1.36)**	**-0.84 (-1.46 to -0.23)**	0	-0.38 (-1.62 to 0.86)	-0.07 (-0.80 to 0.66)
Physical Functioning	**-4.62 (-6.83 to -2.42)**	**-2.32 (-4.19 to -0.46)**	**-0.92 (-1.71 to -0.14)**	0	-0.03 (-1.59 to 1.54)	-0.37 (-1.71 to 0.96)
Role Physical	**-3.65 (-6.01 to -1.28)**	**-2.34 (-3.76 to -0.91)**	-1.08 (-2.30 to 0.14)	0	-0.31 (-1.28 to 0.65)	0.03 (-1.36 to 1.42)
Bodily Pain	**-2.59 (-4.23 to -0.94)**	**-1.91 (-3.69 to -0.14)**	-0.27 (-0.92 to 0.37)	0	-0.91 (-2.36 to 0.54)	0.01 (-1.40 to 1.42)
General Health	**-3.27 (-4.76 to -1.79)**	**-2.06 (-3.54 to -0.57)**	-0.35 (-1.59 to 0.89)	0	0.16 (-1.07 to 1.39)	0.56 (-0.25 to 1.38)
Mental Components	-0.17 (-2.32 to 1.98)	0.09 (-1.07 to 1.24)	0.03 (-0.57 to 0.63)	0	0.11 (-0.62 to 0.84)	0.38 (-0.46 to 1.23)
Mental Health	-0.92 (-2.75 to 0.91)	-0.15 (-0.72 to 0.42)	0.22 (-0.62 to 1.06)	0	0.09 (-1.06 to 1.25)	0.49 (-0.63 to 1.60)
Role Emotional	**-1.73 (-3.33 to -0.14)**	-0.61 (-1.84 to 0.63)	**-0.82 (-1.59 to -0.05)**	0	-0.08 (-0.85 to 0.69)	-0.15 (-1.04 to 0.75)
Social Functioning	-1.03 (-2.55 to 0.49)	-0.76 (-2.40 to 0.88)	-0.08 (-0.48 to 0.33)	0	0.06 (-1.20 to 1.31)	0.12 (-1.27 to 1.50)
Vitality	**-2.17 (-3.41 to -0.93)**	**-1.75 (-2.25 to -1.25)**	-0.32 (-0.73 to 0.10)	0	-0.21 (-0.77 to 0.36)	0.46 (-0.12 to 1.05)

Δ Linear regression coefficient: It represents the difference in QOL score between a given ABI category to the reference category (1.10-1.19). Negative coefficient means lower QOL score in the given category comparing to the reference group. Red & bold indicates statistically significant results.

† Model 2 covariates: age, sex, ethnicity, education level, self-indicated economics status, body mass index, current smoking status, current drinking status, total cholesterol level, diabetes, hypertension, history of CHD, history of heart failure and history of stroke

Supplementary Table 4. Odds-ratio of other QOL parameters across ABI categories using Model 1†.

Other QOL Parameters	ABI categories† (n)					
	<0.90 (402)	0.90-0.99 (426)	1.00-1.09 (1,234)	1.10-1.19 (1,900)	1.20-1.29 (694)	≥1.30 (459)
	OR$^{\Delta}$ (95% CI)	OR (95% CI)	OR (95% CI)	Ref	OR (95% CI)	OR (95% CI)
Physical Activity						
"Low" leisure time exercise	**1.51 (1.20 to 1.90)**	**1.54 (1.06 to 2.23)**	**1.28 (1.13 to 1.45)**	1	1.01 (0.80 to 1.28)	1.01 (0.71 to 1.42)
"Low" leisure time activity	**1.74 (1.51 to 2.01)**	**1.58 (1.36 to 1.83)**	**1.26 (1.11 to 1.42)**	1	**0.74 (0.59 to 0.92)**	0.90 (0.67 to 1.20)
"Low" leisure time walk	**1.62 (1.42 to 1.85)**	**1.56 (1.17 to 2.09)**	**1.31 (1.16 to 1.49)**	1	0.93 (0.76 to 1.13)	0.99 (0.84 to 1.16)
Mental Health						
Depression	**1.97 (1.14 to 3.41)**	**1.46 (1.00 to 2.14)**	**1.32 (1.10 to 1.59)**	1	0.78 (0.48 to 1.27)	1.02 (0.65 to 1.61)
Hopeless Feeling	**1.33 (1.10 to 1.61)**	**1.37 (1.26 to 1.50)**	**1.39 (1.03 to 1.88)**	1	0.91 (0.64 to 1.30)	1.02 (0.56 to 1.84)

Δ Logistic regressions were applied to assess the 5 binary other QOL parameters. Red & bold indicates statistically significant results.

† Model 1 covariates: age, sex, ethnicity, education level, self-indicated economics status.

Supplementary Table 5. Odds-ratio of other QOL parameters across ABI categories using Model 2†.

Other QOL Parameters	ABI categories† (n)					
	<0.90 (402)	0.90-0.99 (426)	1.00-1.09 (1,234)	1.10-1.19 (1,900)	1.20-1.29 (694)	≥1.30 (459)
	OR$^{\Delta}$ (95% CI)	OR (95% CI)	OR (95% CI)	Ref	OR (95% CI)	OR (95% CI)
Physical Activity						
"Low" leisure time exercise	**1.38 (1.12 to 1.71)**	1.41 (1.00 to 1.99)	**1.22 (1.10 to 1.36)**	1	1.01 (0.79 to 1.29)	0.95 (0.68 to 1.33)
"Low" leisure time activity	**1.51 (1.38 to 1.66)**	**1.36 (1.18 to 1.57)**	**1.17 (1.09 to 1.27)**	1	**0.73 (0.60 to 0.90)**	0.78 (0.58 to 1.04)
"Low" leisure time walk	**1.50 (1.33 to 1.69)**	**1.44 (1.14 to 1.82)**	**1.26 (1.13 to 1.42)**	1	0.93 (0.77 to 1.12)	0.92 (0.79 to 1.07)
Mental Health						
Depression	1.76 (0.99 to 3.13)	1.32 (0.85 to 2.03)	**1.27 (1.04 to 1.56)**	1	0.78 (0.47 to 1.28)	0.92 (0.60 to 1.42)
Hopeless Feeling	**1.21 (1.01 to 1.45)**	**1.27 (1.12 to 1.44)**	1.35 (0.99 to 1.83)	1	0.91 (0.63 to 1.30)	0.95 (0.53 to 1.71)

Δ Logistic regressions were applied to assess the 5 binary other QOL parameters. Red & bold indicates statistically significant results.

† Model 2 covariates: age, sex, ethnicity, education level, self-indicated economics status, body mass index, current smoking status, current drinking status, total cholesterol level, diabetes, hypertension, history of CHD, history of heart failure and history of stroke.

Supplementary Table 6. The difference in Physical Component Summary scores across ABI categories in different subgroups.

Subgroups	ABI categories† (n)					
	<0.90	0.90-0.99	1.00-1.09	1.10-1.19	1.20-1.29	≥1.30
	Coefficient$^{\Delta}$ (95% CI)	Coefficient (95% CI)	Coefficient (95% CI)	Ref	Coefficient (95% CI)	Coefficient (95% CI)
Sex*						
Males	-3.84 (-8.25 to 0.57)	-1.72 (-3.68 to 0.24)	-0.46 (-1.90 to 0.98)	0	0.57 (-0.30 to 1.45)	0.28 (-1.01 to 1.56)
Females	-2.56 (-5.39 to 0.27)	**-2.44 (-4.41 to -0.48)**	-0.74 (-2.20 to 0.73)	0	-1.88 (-4.33 to 0.58)	-0.45 (-2.73 to 1.83)
P value for interaction	**0.014**					
Ethnicity						
Caucasian	**-3.68 (-7.13 to -0.23)**	-2.00 (-4.53 to 0.53)	-0.48 (-1.40 to 0.45)	0	-0.37 (-0.87 to 0.12)	0.05 (-0.90 to 1.00)
African American	**-3.05 (-3.78 to -2.31)**	**-2.73 (-3.79 to -1.68)**	**-0.88 (-1.49 to -0.27)**	0	-2.47 (-6.31 to 1.36)	**-1.54 (-3.01 to -0.07)**
P value for interaction	0.051					
CVD History*						
No CVD history	**-4.54 (-7.70 to -1.38)**	-2.56 (-5.23 to 0.10)	-0.67 (-1.73 to 0.39)	0	-0.96 (-2.29 to 0.38)	-0.42 (-2.20 to 1.36)
CVD history	-1.10 (-2.82 to 0.62)	-1.01 (-3.62 to 1.60)	-0.22 (-1.15 to 0.71)	0	1.58 (-0.64 to 3.80)	1.20 (-2.02 to 4.41)
P value for interaction	**0.001**					
Diabetes						
No Diabetes	**-3.60 (-7.10 to -0.09)**	**-2.56 (-4.81 to -0.31)**	-0.95 (-2.64 to 0.74)	0	-1.05 (-2.43 to 0.33)	-0.39 (-1.76 to 0.98)
Diabetes	**-2.37 (-3.20 to -1.53)**	-1.32 (-5.83 to 3.18)	0.19 (-1.25 to 1.64)	0	0.63 (-0.88 to 2.14)	0.71 (-1.52 to 2.94)
P value for interaction	0.388					
Reduced Kidney Function						
Not Reduced	**-3.33 (-5.59 to -1.06)**	**-2.78 (-4.79 to -0.77)**	**-1.26 (-2.46 to -0.07)**	0	-1.00 (-2.16 to 0.17)	-0.04 (-1.64 to 1.56)
Reduced	**-2.86 (-5.40 to -0.31)**	-0.87 (-2.94 to 1.20)	1.14 (-0.14 to 2.43)	0	0.84 (-2.85 to 4.52)	-0.26 (-1.66 to 1.13)
P value for interaction	0.096					

Δ Linear regression coefficient: It represents the difference in Mental Component Summary score between ABI category <1.00 and the reference category (≥1.00), adjusted for all covariates. Negative coefficient means lower Mental Component Summary score in the ABI category <1.00 comparing to the reference group. Red & bold indicates statistically significant results. Global F test were used to test significant interaction terms.

Supplementary Table 7. The difference in Mental Component Summary scores across ABI categories in different subgroups

Subgroups	ABI categories† (n)					
	<0.90	0.90-0.99	1.00-1.09	1.10-1.19	1.20-1.29	≥1.30
	Coefficient$^{\Delta}$ (95% CI)	Coefficient (95% CI)	Coefficient (95% CI)	Ref	Coefficient (95% CI)	Coefficient (95% CI)
Sex						
Males	0.27 (-2.23 to 2.78)	-0.71 (-2.16 to 0.75)	0.62 (-0.20 to 1.44)	0	0.19 (-1.01 to 1.40)	0.19 (-0.74 to 1.12)
Females	-0.36 (-2.21 to 1.48)	0.47 (-1.46 to 2.40)	-0.20 (-0.88 to 0.49)	0	0.06 (-1.90 to 2.02)	0.95 (-0.74 to 2.64)
P value for interaction	0.28					
Ethnicity						
Caucasian	-0.39 (-2.85 to 2.07)	0.09 (-1.37 to 1.55)	0.20 (-0.41 to 0.81)	0	0.26 (-0.27 to 0.80)	0.58 (-0.15 to 1.31)
African American	0.24 (-1.55 to 2.04)	0.14 (-0.55 to 0.83)	-0.41 (-2.08 to 1.25)	0	-0.73 (-1.89 to 0.43)	**-0.50 (-1.00 to -0.01)**
P value for interaction	0.152					
CVD History						
No CVD history	-0.39 (-2.87 to 2.10)	0.39 (-0.84 to 1.61)	0.04 (-0.63 to 0.71)	0	0.24 (-0.42 to 0.91)	0.35 (-0.58 to 1.28)
CVD history	0.29 (-1.57 to 2.16)	-0.53 (-1.68 to 0.63)	0.20 (-1.39 to 1.79)	0	-0.81 (-2.39 to 0.77)	0.31 (-0.14 to 0.76)
P value for interaction	**0.011**					
Diabetes						
No Diabetes	-0.37 (-1.73 to 1.00)	0.09 (-1.25 to 1.44)	-0.05 (-1.21 to 1.11)	0	0.30 (-0.08 to 0.67)	0.47 (-1.14 to 2.09)
Diabetes	0.36 (-2.86 to 3.57)	0.61 (-2.23 to 3.45)	0.33 (-1.87 to 2.53)	0	-0.27 (-2.17 to 1.63)	0.31 (-1.13 to 1.76)
P value for interaction	0.976					
Reduced Kidney Function						
Not Reduced	0.31 (-2.78 to 3.41)	**0.59 (0.09 to 1.08)**	0.44 (-0.22 to 1.10)	0	0.22 (-0.19 to 0.64)	0.37 (-1.09 to 1.83)
Reduced	-0.96 (-3.85 to 1.93)	-0.85 (-2.84 to 1.14)	-0.99 (-2.60 to 0.61)	0	-0.35 (-3.59 to 2.89)	0.19 (-0.84 to 1.21)
P value for interaction	**0.031**					

Δ Linear regression coefficient: It represents the difference in Mental Component Summary score between ABI category <1.00 and the reference category (≥1.00), adjusted for all covariates. Negative coefficient means lower Mental Component Summary score in the ABI category <1.00 comparing to the reference group. Red & bold indicates statistically significant results. Global F test were used to test significant interaction terms.

Supplementary Table 8. Odds-ratio of other physical activity parameters for lower ABI (<1.00) in different subgroups.

Subgroups	Physical Activity Parameters					
	"Low" leisure time exercise		"Low" leisure time activity		"Low" leisure time walk	
	Case/N†	OR$^{\Delta}$ (95% CI)	Case/N	OR$^{\Delta}$ (95% CI)	Case/N	OR (95% CI)
Sex						
Males	162/316	1.30 (0.91 to 1.87)	56/316	1.10 (0.81 to 1.48)	104/316	**1.34 (1.05 to 1.71)**
Females	316/512	**1.25 (1.04 to 1.50)**	148/512	**1.41 (1.18 to 1.69)**	216/512	**1.30 (1.18 to 1.43)**
P value for interaction		0.854		0.661		0.629
Ethnicity						
Caucasian	314/531	**1.38 (1.01 to 1.88)**	122/531	**1.29 (1.14 to 1.47)**	206/531	**1.38 (1.14 to 1.66)**
African American	164/297	1.10 (0.98 to 1.23)	82/297	**1.27 (1.24 to 1.30)**	114/297	**1.18 (1.07 to 1.30)**
P value for interaction		0.150		0.686		0.278
CVD History						
No CVD history	329/565	**1.31 (1.01 to 1.70)**	149/565	**1.50 (1.34 to 1.69)**	226/565	**1.41 (1.24 to 1.61)**
CVD history	149/263	1.17 (0.91 to 1.51)	55/263	0.96 (0.69 to 1.32)	94/263	1.08 (0.84 to 1.39)
P value for interaction		0.185		**0.007**		**< 0.001**
Diabetes						
No Diabetes	276/513	1.14 (0.83 to 1.56)	111/513	**1.47 (1.04 to 2.07)**	192/513	**1.40 (1.04 to 1.88)**
Diabetes	202/315	**1.57 (1.21 to 2.03)**	93/315	1.08 (0.79 to 1.48)	128/315	1.18 (0.88 to 1.57)
P value for interaction		0.315		0.262		0.352
Reduced Kidney Function						
Not Reduced	283/492	**1.35 (1.06 to 1.71)**	117/492	**1.42 (1.24 to 1.62)**	176/492	**1.35 (1.17 to 1.56)**
Reduced	195/336	1.15 (0.86 to 1.53)	87/336	1.15 (0.88 to 1.50)	144/336	1.26 (1.04 to 1.53)
P value for interaction		0.383		0.069		0.662

† Number of individuals having outcome with ABI < 1.00 for each subgroup/ Total number of individuals with ABI < 1.00 for each subgroup

Δ Logistic regressions were applied to assess the ratio of odds for 3 binary physical activity parameters between ABI category <1.00 and the reference category (≥1.00). Red & bold indicates statistically significant results.

Supplementary Table 9. Odds-ratio of other mental health parameters for lower ABI (<1.00) in different subgroups.

Subgroups	Mental Health Parameters			
	Depression		Hopeless feeling	
	Case/N †	OR$^{\Delta}$ (95% CI)	Case/N	OR (95% CI)
Sex				
Males	24/316	1.22 (0.62 to 2.39)	37/316	1.09 (0.84 to 1.42)
Females	57/512	1.29 (0.68 to 2.43)	74/512	1.04 (0.78 to 1.40)
P value for interaction		0.809		0.289
Ethnicity				
Caucasian	51/531	**1.65 (1.05 to 2.59)**	70/531	**1.23 (1.10 to 1.36)**
African American	30/297	**0.84 (0.74 to 0.96)**	41/297	**0.83 (0.78 to 0.88)**
P value for interaction		**0.001**		**< 0.001**
CVD History				
No CVD history	52/565	1.20 (0.69 to 2.09)	77/565	1.06 (0.70 to 1.59)
CVD history	29/263	1.50 (0.88 to 2.58)	34/263	1.11 (0.79 to 1.57)
P value for interaction		**0.036**		0.936
Diabetes				
No Diabetes	40/513	1.23 (0.51 to 2.94)	64/513	1.15 (0.89 to 1.50)
Diabetes	41/315	1.28 (0.81 to 2.02)	47/315	0.91 (0.61 to 1.37)
P value for interaction		0.975		0.070
Reduced Kidney Function				
Not Reduced	41/492	1.11 (0.70 to 1.75)	61/492	1.05 (0.73 to 1.51)
Reduced	40/336	1.63 (0.73 to 3.62)	50/336	1.07 (0.81 to 1.40)
P value for interaction		0.271		0.809

† Number of individuals having outcome with ABI < 1.00 for each subgroup / Total number of individuals with ABI < 1.00 for each subgroup

Δ Logistic regressions were applied to assess the ratio of odds for 2 binary mental health parameters between ABI category <1.00 and the reference category (≥1.00). Red & bold indicates statistically significant results.

BIBLIOGRAPHIES

1. Adesunloye BA, Valadri R, Mbaezue NM, Onwuanyi AE. Impact of peripheral arterial disease on functional limitation in congestive heart failure: Results from the national health and nutrition examination survey (1999-2004). *Cardiol. Res. Pract.* 2012;2012:306852
2. Fleg JL, Forman DE, Berra K, Bittner V, Blumenthal JA, Chen MA, Cheng S, Kitzman DW, Maurer MS, Rich MW, Shen WK, Williams MA, Zieman SJ. Secondary prevention of atherosclerotic cardiovascular disease in older adults: A scientific statement from the american heart association. *Circulation*. 2013;128:2422-2446
3. Selvin E, Erlinger TP. Prevalence of and risk factors for peripheral arterial disease in the united states: Results from the national health and nutrition examination survey, 1999-2000. *Circulation*. 2004;110:738-743
4. Ostchega Y, Paulose-Ram R, Dillon CF, Gu Q, Hughes JP. Prevalence of peripheral arterial disease and risk factors in persons aged 60 and older: Data from the national health and nutrition examination survey 1999-2004. *Journal of the American Geriatrics Society*. 2007;55:583-589
5. Murabito JM, Evans JC, Larson MG, Nieto K, Levy D, Wilson PW. The ankle-brachial index in the elderly and risk of stroke, coronary disease, and death: The framingham study. *Archives of internal medicine*. 2003;163:1939-1942
6. Minar E. Critical limb ischaemia. *Hämostaseologie*. 2009;29:102-109
7. Heald CL, Fowkes FG, Murray GD, Price JF. Risk of mortality and cardiovascular disease associated with the ankle-brachial index: Systematic review. *Atherosclerosis*. 2006;189:61-69
8. Roger VL, Go AS, Lloyd-Jones DM, Benjamin EJ, Berry JD, Borden WB, Bravata

DM, Dai S, Ford ES, Fox CS, Fullerton HJ, Gillespie C, Hailpern SM, Heit JA, Howard VJ, Kissela BM, Kittner SJ, Lackland DT, Lichtman JH, Lisabeth LD, Makuc DM, Marcus GM, Marelli A, Matchar DB, Moy CS, Mozaffarian D, Mussolino ME, Nichol G, Paynter NP, Soliman EZ, Sorlie PD, Sotoodehnia N, Turan TN, Virani SS, Wong ND, Woo D, Turner MB. Heart disease and stroke statistics--2012 update: A report from the american heart association. *Circulation*. 2012;125:e2-e220

9. Norgren L, Hiatt WR, Dormandy JA, Nehler MR, Harris KA, Fowkes FGR. Inter-society consensus for the management of peripheral arterial disease (tasc ii). *Journal of Vascular Surgery*.45:S5-S67

10. McDermott MM, Liu K, Greenland P, Guralnik JM, Criqui MH, Chan C, Pearce WH, Schneider JR, Ferrucci L, Celic L, Taylor LM, Vonesh E, Martin GJ, Clark E. Functional decline in peripheral arterial disease: Associations with the ankle brachial index and leg symptoms. *JAMA : the journal of the American Medical Association*. 2004;292:453-461

11. Dumville JC, Lee AJ, Smith FB, Fowkes FG. The health-related quality of life of people with peripheral arterial disease in the community: The edinburgh artery study. *The British journal of general practice : the journal of the Royal College of General Practitioners*. 2004;54:826-831

12. McDermott MM, Greenland P, Liu K, Guralnik JM, Criqui MH, Dolan NC, Chan C, Celic L, Pearce WH, Schneider JR, Sharma L, Clark E, Gibson D, Martin GJ. Leg symptoms in peripheral arterial disease: Associated clinical characteristics and functional impairment. *JAMA : the journal of the American Medical Association*. 2001;286:1599-1606

13. Chetter IC, Spark JI, Dolan P, Scott DJ, Kester RC. Quality of life analysis in patients with lower limb ischaemia: Suggestions for european standardisation.

European journal of vascular and endovascular surgery : the official journal of the European Society for Vascular Surgery. 1997;13:597-604

14. Amer MS, Alsadany MA, Tolba MF, Omar OH. Quality of life in elderly diabetic patients with peripheral arterial disease. *Geriatr Gerontol Int*. 2013;13:443-450
15. Breek JC, Hamming JF, De Vries J, Aquarius AEAM, van Berge Henegouwen DP. Quality of life in patients with intermittent claudication using the world health organisation (who) questionnaire. *European Journal of Vascular and Endovascular Surgery*. 2001;21:118-122
16. Butler RN. Towards a definition of quality of life for an aging society. *In Symposium report: The Quality of Life in Old Age: Views from Various Cultural Perspectives. New York: International Longevity Center*. 1997
17. Study TARiCA. Manual 2 home and field center procedures aric visit 5 and ncs study protocol. 2013
18. Allison MA, Laughlin GA, Barrett-Connor E, Langer R. Association between the ankle-brachial index and future coronary calcium (the rancho bernardo study). *Am. J. Cardiol.* 2006;97:181-186
19. Ix JH, Katz R, Peralta CA, de Boer IH, Allison MA, Bluemke DA, Siscovick DS, Lima JAC, Criqui MH. A high ankle brachial index is associated with greater left ventricular mass: The multi-ethnic study of atherosclerosis. *Journal of the American College of Cardiology*. 2010;55:342-349
20. Wattanakit K, Folsom AR, Duprez DA, Weatherley BD, Hirsch AT. Clinical significance of a high ankle-brachial index: Insights from the atherosclerosis risk in communities (aric) study. *Atherosclerosis*. 2007;190:459-464
21. Gandek B, Ware JE, Aaronson NK, Apolone G, Bjorner JB, Brazier JE, Bullinger M, Kaasa S, Leplege A, Prieto L, Sullivan M. Cross-validation of item selection and scoring for the sf-12 health survey in nine countries: Results from the iqola

project. International quality of life assessment. *J. Clin. Epidemiol.* 1998;51:1171-1178

22. Sanderson K, Andrews G. The sf-12 in the australian population: Cross-validation of item selection. *Aust. N. Z. J. Public Health*. 2002;26:343-345
23. Ware J, Jr., Kosinski M, Keller SD. A 12-item short-form health survey: Construction of scales and preliminary tests of reliability and validity. *Med. Care*. 1996;34:220-233
24. Ware JEJ. Sf-36 health survey manual and interpretation guide. *Boston: The Health Institute, New England Medical Center*. 1996
25. Kohout FJ, Berkman LF, Evans DA, Cornoni-Huntley J. Two shorter forms of the ces-d (center for epidemiological studies depression) depression symptoms index. *J. Aging Health*. 1993;5:179-193
26. Gellis ZD. Assessment of a brief ces-d measure for depression in homebound medically ill older adults. *Journal of gerontological social work*. 2010;53:289-303
27. Lutsey PL, Rasmussen-Torvik LJ, Pankow JS, Alonso A, Smolenski DJ, Tang W, Coresh J, Volcik KA, Ballantyne CM, Boerwinkle E, Folsom AR. Relation of lipid gene scores to longitudinal trends in lipid levels and incidence of abnormal lipid levels among individuals of european ancestry: The atherosclerosis risk in communities (aric) study. *Circ. Cardiovasc. Genet.* 2012;5:73-80
28. Schroeder EB, Chambless LE, Liao D, Prineas RJ, Evans GW, Rosamond WD, Heiss G. Diabetes, glucose, insulin, and heart rate variability: The atherosclerosis risk in communities (aric) study. *Diabetes Care*. 2005;28:668-674
29. Luft VC, Pereira M, Pankow JS, Ballantyne C, Couper D, Heiss G, Duncan BB. Retinol binding protein 4 and incident diabetes--the atherosclerosis risk in communities study (aric study). *Revista brasileira de epidemiologia = Brazilian journal of epidemiology*. 2013;16:388-397

30. Rooke TW, Hirsch AT, Misra S, Sidawy AN, Beckman JA, Findeiss LK, Golzarian J, Gornik HL, Halperin JL, Jaff MR, Moneta GL, Olin JW, Stanley JC, White CJ, White JV, Zierler RE. 2011 accf/aha focused update of the guideline for the management of patients with peripheral artery disease (updating the 2005 guideline)a report of the american college of cardiology foundation/american heart association task force on practice guidelines. *Journal of the American College of Cardiology*. 2011;58:2020-2045

31. McDermott MM, Applegate WB, Bonds DE, Buford TW, Church T, Espeland MA, Gill TM, Guralnik JM, Haskell W, Lovato LC, Pahor M, Pepine CJ, Reid KF, Newman A. Ankle brachial index values, leg symptoms, and functional performance among community-dwelling older men and women in the lifestyle interventions and independence for elders study. *Journal of the American Heart Association*. 2013;2:e000257

32. Fowkes FG, Murray GD, Butcher I, Heald CL, Lee RJ, Chambless LE, Folsom AR, Hirsch AT, Dramaix M, deBacker G, Wautrecht JC, Kornitzer M, Newman AB, Cushman M, Sutton-Tyrrell K, Fowkes FG, Lee AJ, Price JF, d'Agostino RB, Murabito JM, Norman PE, Jamrozik K, Curb JD, Masaki KH, Rodriguez BL, Dekker JM, Bouter LM, Heine RJ, Nijpels G, Stehouwer CD, Ferrucci L, McDermott MM, Stoffers HE, Hooi JD, Knottnerus JA, Ogren M, Hedblad B, Witteman JC, Breteler MM, Hunink MG, Hofman A, Criqui MH, Langer RD, Fronek A, Hiatt WR, Hamman R, Resnick HE, Guralnik J, McDermott MM. Ankle brachial index combined with framingham risk score to predict cardiovascular events and mortality: A meta-analysis. *JAMA : the journal of the American Medical Association*. 2008;300:197-208

33. Korhonen PE, Seppala T, Kautiainen H, Jarvenpaa S, Aarnio PT, Kivela SL. Ankle-brachial index and health-related quality of life. *European journal of*

preventive cardiology. 2012;19:901-907

34. Inglis SC, Lewsey JD, Lowe GD, Jhund P, Gillies M, Stewart S, Capewell S, Macintyre K, McMurray JJ. Angina and intermittent claudication in 7403 participants of the 2003 scottish health survey: Impact on general and mental health, quality of life and five-year mortality. *Int. J. Cardiol.* 2013;167:2149-2155
35. Regensteiner JG, Hiatt WR, Coll JR, Criqui MH, Treat-Jacobson D, McDermott MM, Hirsch AT. The impact of peripheral arterial disease on health-related quality of life in the peripheral arterial disease awareness, risk, and treatment: New resources for survival (partners) program. *Vascular medicine (London, England)*. 2008;13:15-24
36. Cluff K, Kelly AM, Koutakis P, He XN, Huang X, Lu YF, Pipinos, II, Casale GP, Subbiah J. Surface-enhanced raman spectral biomarkers correlate with ankle brachial index and characterize leg muscle biochemical composition of patients with peripheral arterial disease. *Physiological reports*. 2014;2
37. Lane RA, Mazari F, Mockford KA, Vanicek N, Chetter IC, Coughlin PA. Fear of falling in claudicants and its relationship to physical ability, balance, and quality of life. *Vasc. Endovascular Surg.* 2014;48:297-304

CURRICULUM VITAE

Aozhou Wu

Johns Hopkins Bloomberg School of Public Health, Baltimore, MD
Mobile: 1-410-736-2558 Email: wuaozhou@gmail.com

PROFILE

Master degree student at the Johns Hopkins Bloomberg School of Public Health in General Epidemiology and Methodology with training previous in medicine and statistics. Currently doing research on chronic kidney disease and peripheral artery disease and working as a research assistant. Planning to further develop expertise in epidemiology and statistical methods applied to cardiovascular disease with the long-term goal of doing research to improve public health globally.

EDUCATION

Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, US

- ***Master of Health Science***, expected 2015 Major in General Epidemiology and Methodology
  GPA: 4.00/4.00 (Till current term)
  Thesis: "Lower Extremity Peripheral Artery Disease and Quality of Life among Older Individuals in the Community: The Atherosclerosis Risk in Communities (ARIC) Study"

Peking University Health Science Center, Beijing, China

- ***Bachelor of Medicine***, 2013 Major in Laboratory Medicine
  GPA: 3.85/4.00
- ***Bachelor of Science*** in Statistics, 2013

RESEARCH EXPERIENCE

Research Assistant, Dept. of Epidemiology, Johns Hopkins School of Public Health, US
Feb. 2014 - Current

Mortality prediction in chronic kidney disease patients

- Supervised by Dr. Kunihiro Matsushita and Dr. Tariq Shafi
- Developed risk prediction models for all cause mortality/ CVD death/ sudden cardiac death, via Cox Proportional Hazard model /Competing risk model, selecting from over 40 traditional predictors and novel biomarkers in CHOICE study.

- Evaluated final models by Hosmer-lemeshow goodness of fit test statistic, net reclassification index and Jackknife cross-validation of the results.
- Paper under preparation.

Quality of life among persons with chronic kidney disease and critical limb ischemia in ARIC study

- Student investigator, supervised by Dr. Kunihiro Matsushita
- Assess the association between critical limb ischemia and quality of life and the role of chronic kidney disease in this association in ARIC cohort.
- Abstract accepted for a poster presentation by AHA EPI/Lifestyle conference in 2015.

Research Assistant, National Center for AIDS/STD Control and Prevention, China CDC, China
Jan 2012 - June 2013

Hepatitis C (HCV) and HCV-HIV co-infection status in participants of national methadone maintenance treatment program

- Supervised by Dr. Enwu Liu
- Conduct descriptive and survival analysis to assess the prevalence, incidence and related risk factors for participants in national methadone maintenance treatment program. Contributed to drafting a manuscript.

Lab Assistant, Department of Pharmacy, Peking University Health Science Center, China
Jan 2010 -July 2011

- Supervised by Dr. Qing Xia
- Conducted basic experiments of Dr. Qing Xia's projects on neuron ischemia-reperfusion injury.
- Translated parts of a research related book on blood-brain barrier and made report on the summary of translated parts.

INTERNSHIP EXPERIENCE

Head intern, Dept. of Laboratory Medicine, Peking University People's Hospital, China
Aug 2012 – May 2013

- Supervised by Dr. Hui Wang
- Arranged intern shifting among sub-departments, coordinated with doctors, instructors and interns
- Participated biochemistry lab analysis, blood/urine/face tests, etc.

Lab intern, Dept. of Neuroscience, Peking University Health Science Center, China
Nov 2011- Mar 2012

- Supervised by Dr. Yun Wang
- Participated in research concerning pain release mechanism
- Presented a literature report on *Molecule Mechanism under Pain*

Intern, The Joint United Nations Program on HIV/AIDS (UNAIDS) in China, Beijing, China

Aug 2010

- Organized training materials for gender workshop and slides on HIV epidemic and response
- Completed an analytical report on HIV status in Chongqing, China

SOCIAL EXPERIENCE

Class monitor, Peking University Health Science Center, Beijing, China
Sep 2009 – July 2013

- Ran routine class affairs, coordinated with courses instructors and teaching assistants
- Organized class activities, such as museum visit, spring hiking, sports competition, etc.

Project manager, Junior Achievement (JA) institution, Beijing, China
Oct 2009 - May 2011

- Arranged and promoted JA courses, recruited students and instructors
- Planned and implemented institution activities, such as mock interviews, career development, etc.

HONORS, AWARDS & SCHOLARSHIPS

- Merit Student Award of Peking University (awarded for consecutive three years) 2009-2011
- Peking University First-Class Scholarship of Medical Student
  Sep 2009 - July 2010
- The May Fourth Scholarship
  Sep 2010 - July 2011
- National Scholarship
  Sep 2011 - July 2012

PUBLICATION IN PREPARATION

- Kruzan R, Parekh RS, Herzog C, **Wu A**, Powe N, Coresh J, Matsushita K, Shafi T. Association of Troponin I and NTproBNP with Outpatient Sudden Cardiac Death in Hemodialysis Patients. *Plan to submit to Circulation.*
- **Aozhou Wu**, Josef Coresh, Elizabeth Selvin, Hirofumi Tanaka, Gerardo Heiss, Alan T. Hirsch, Bernard Jaar, Kunihiro Matsushita. Lower Extremity Peripheral Artery Disease and Quality of Life among Older Individuals in the Community: The Atherosclerosis Risk in Communities (ARIC) Study. *Abstract accepted for a poster presentation by AHA EPI/Lifestyle conference in 2015 and the paper is under writing.*